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EFFECTS OF HIGH CONCENTRATIONS OF CARBON DIOXIDE AND DIET ON URINARY EXCRETION OF STEROIDS AND CATECHOLAMINES,

AEROSPACE MEDICAL DIV BROOKS AFB TX

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FOREWORD

This report was prepared by the following personnel in the Environmental Systems Section:

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ABSTRACT

Air Force pilots were exposed to inspired tracheal P_{CO_2} of 21 mm. Hg (BTPS) at 700 mm. Hg and 200 mm. Hg cabin pressure. Each exposure was of 4 days' duration and was preceded in each case by a control period of low CO_2 also of 4 days' duration at the equivalent cabin pressures. During the entire experiment, including pre- and postexperiment control periods, the subjects were given a special liquid diet. The effects of CO_2 and diet on the endocrine functions were studied by determining the urinary excretion of epinephrine, norepinephrine, 17-OHCS, and corticosterone-like hormones. It was found that the CO_2, both at ground and at simulated altitude, increased the excretion of epinephrine, norepinephrine, and corticosterone-like hormones. CO_2 at simulated altitude had a stronger effect than at ground level. The special liquid diet caused increased excretion of epinephrine, while the excretion of the other three hormone groups decreased.

This technical documentary report has been reviewed and is approved.

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EFFECTS OF HIGH CONCENTRATIONS OF CARBON DIOXIDE AND DIET ON URINARY EXCRETION OF STEROIDS AND CATECHOLAMINES

1. INTRODUCTION

It has become increasingly important to know the effects of carbon dioxide on man when he is exposed to artificial atmospheres for prolonged time. In future space travels, the astronaut will of necessity be restricted to a closed environment where the gaseous composition of the atmosphere is mechanically controlled. Space travelers may be exposed to concentrations of CO_2 higher than what is considered the upper limit of tolerance. The carbon dioxide removal system in the spacecraft, be it chemical or physical, may fail or be overtaxed owing to increased production of the gas by the crew members. It is, therefore, imperative that we learn the tolerance limits for carbon dioxide and the physiology of man exposed to carbon dioxide at reduced atmospheric pressure. Chronic tolerance studies of carbon dioxide exposure at sea level atmosphere have been undertaken by several investigators (14, 21), and at least one study (1) has been made at decreased pressure accompanied by increased concentrations of carbon dioxide. In the latter study, hypoxic hyperventilation was superimposed on any carbon dioxide effect, and the experiment was of short duration. These earlier studies are not strictly applicable to the reduced pressure with enriched oxygen atmosphere proposed for future spacecraft travels of long duration. A series of experiments was, therefore, designed to study man's physiologic response and tolerance to carbon dioxide in a space-equivalent environment. Reports (including ref. 4) from this laboratory will deal with the various aspects of the study. Since it has been indicated that the endocrine activity is affected by increased concentrations of carbon dioxide (7), this report will deal mainly with the excretion of steroids and catecholamines from subjects exposed to increased concentrations of carbon dioxide in an oxygen-rich atmosphere at less than sea level pressure.

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2. METHOD

An altitude indoctrination chamber was adapted to obtain the desired sensitivity and control over the gaseous and other environmental parameters of interest. Eight volunteer test subjects, all healthy, young Air Force pilots, were exposed to four atmospheric compositions and pressures (table I). The duration of exposure in each atmosphere was four days in the sequence listed in table IA. After being exposed to the carbon dioxide–rich atmosphere at 700 mm. Hg pressure, the subjects were removed from the chamber for 4 days to permit recovery studies prior to the exposure to the 200 mm. Hg pressure atmospheres. For a period of 4 days before entering the chamber for the first time, until 4 days after the last day in the chamber, the subjects were on a special liquid diet which will be described later. Furthermore, a normal dietary control period preceded and followed the liquid diet control periods; each of these periods also lasted 4 days.

Carbon dioxide was monitored by a Beckman LB-1 infrared analyzer; oxygen was monitored by a Beckman F-3 analyzer. Recalibration was performed every 12 hours but actual gas readings were taken every 15 minutes; average values are presented in table I. It should be mentioned that BTPS conditions were used to derive comparable CO_2 values that

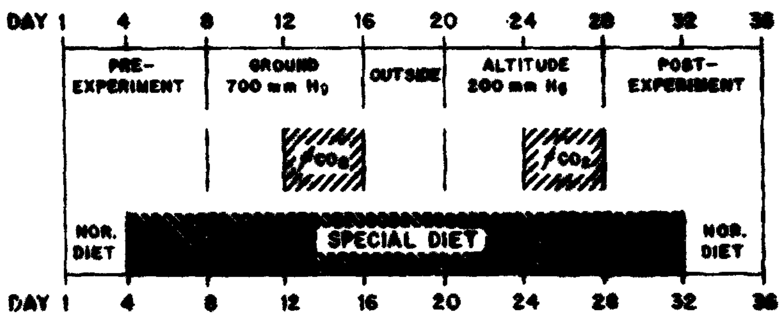
TABLE I

Environmental data for the carbon dioxide experiments

Environmental condition	1 Low altitude - Low CO_2	2 Low altitude - High CO_2	3 High altitude - Low CO_2	4 High altitude - High CO_2
Absolute pressure (mm.Hg)	700	700	200	200
Range	(694-701)	(699-701)	(199.5-201)	(199-200.3)
O_2 concentration (%)	22.7	23.8	92.9	83.0
Range	(21.3-24.5)	(22.0-24.7)	(79.4-98.4)	(76.0-[illegible])
P_{O_2} (BTPS)-tracheal inspired	148.5	155.1	142.7	127.0
CO_2 concentration (%)	0.4	3.3	1.6	13.6
Range	(0.1-1.6)	(2.5-4.3)	(0.1-2.6)	(11.3-15.5)
P_{CO_2} (BTPS)-tracheal inspired	2.5	21.3	2.5	20.9
N_2 concentration (%)	75.6	67.0	1.8	1.8
Range	(69.9-81.5)	(62.5-70.1)	(0.2-5.3)	(0.4-4.7)
P_{N_2} (BTPS)-tracheal inspired	498.7	487.2	2.7	2.7
Temperature (°C.)	24.2	24.2	22.5	22.2
Range	(20.0-27.3)	(20.0-25.9)	(20.0-[illegible])	(20.1-[illegible])
Relative humidity (%)	64.0	80.1	42.6	47.1
Range	(33.3-77.1)	(70.1-89.0)	(23.8-73.4)	(34.2-70.[illegible])
Relative humidity (mm.Hg)	15.0	18.1	8.7	9.5

TABLE IA

Profile of CO_2 experiments



would occur at the two pressures. Also, P_{O_2} (BTPS) was held to similar concentrations in each of the four atmospheric conditions.

The transition from low CO_2 to high CO_2 atmosphere was performed gradually over a 4-hour period. The subjects were not told when or how much CO_2 would be administered, nor what symptoms to expect.

Four days before entering the chamber, the subjects were given a special liquid diet designed by Scrimshaw (13). The diet was composed of oatmeal, toasted soybean flour, powdered skimmed milk, Dexin, vegetable oil, and water with vitamin A and salt added. In addition to this, they were given orange-grapefruit juice mixture enriched with Dexin. This diet gave the subjects 60.4% carbohydrate,

12.0% protein, and 27.6% fat. Of the total calories, 70% came from the food mixture, and 30%, from the juice mixture. The total caloric intake was based on 30 kcal./kg. body weight/day, a figure obtained from previous experiments. In two individuals (Nos. 27 and 28) who lost weight, the caloric intake was increased. Supplementary hard candy and coffee were given and the amount recorded. One subject (No. 28), whose coffee consumption exceeded 33 to 35 grams of instant coffee per day, was given Sanka during the period between the chamber portions of the experiment. Any leftover food was measured and the amount subtracted from the initial food weight. The subjects had their weight and vital signs checked and recorded daily.

The four subjects participating in each of these experiments worked in teams of two. Each team was on duty for 4 hours, then had 1 or 2 hours of free time. Two ground control periods were scheduled from 6:00 to 9:00 a.m. and from 1:00 to 3:00 p.m. to allow for medical evaluation. The schedule was arranged so that one team slept from 1:00 to 6:00 a.m., and the other team slept from 8:00 a.m. to 1:00 p.m. Each man—before, during, and after the experiments—collected urine continuously in 24-hour samples. The collection period started at 7:00 a.m. and lasted to 7:00 a.m. the following morning. As the urine was voided, it was measured, acidified to pH 2 with concentrated HCl, and stored in frozen or refrigerated condition until it was analyzed; delay in analysis was never longer than 48 hours. The steroids were extracted in butanol (2), and 17-OHCS values were determined on a portion of this extract by the Porter-Silber method (10). Corticosterone-like hormones were also analyzed on this extract, by Mader and Buck's blue tetrazolium method (8). Assays were made for both epinephrine and norepinephrine by the trihydroxy-indol method (20).

3. RESULTS

In discussing any possible CO_2 effect on the subjects' physiology, one must keep in mind at least two major considerations: (1) During the initial period inside the chamber, the subjects had to reorganize their way of living and also get accustomed to a new and unusual work schedule. In one of the experiments in this series, there appeared for the first time a personality conflict between two of the subjects and this adversely affected the data during this period. The values for these two subjects, indicated in parentheses in table II, are excluded from the calculations. (2) Being locked in a steel chamber might cause anxiety; the subjects knew that the CO_2 concentration would be increased, but did not know when, how much, or how it would affect them.

As can be seen from the data presented in tables II and III and in figure 2, the subjects showed increased output of all four hormone groups by just going into the chamber at 700 mm. Hg (2,200 feet). This effect was less or even absent when the subjects entered the chamber for the 200 mm. Hg (32,500 feet) portion of the experiment so that the increase seen when the men were in the chamber during the initial period was most likely due to "familiarization strain." How much the personality conflict between the two subjects, which actually lasted for about 4 days, influenced the other two subjects participating in that experiment is unknown. It was thought to be largely responsible for the large increase seen for epinephrine during the initial 4 days in the chamber.

Epinephrine. The overall excretion of epinephrine during the various experimental periods is explainable and follows results obtained by other investigators (12, 17). Values for the two normal-diet control periods were similar, as were values from the three special-diet periods. There was evidence of a chamber effect and an altitude effect with an additional effect on epinephrine excretion in each period the CO_2 concentration was increased (fig. 2). The fact that the increase in epinephrine excretion during the initial period at altitude was considerably less than the excretion during the first chamber period indicates that the subjects had considerable apprehension about the experiment.

TABLE II

Hormone excretions under various experimental conditions

Subject	Normal controls: Normal diet (μg./24 hr.)	Normal controls: Special diet (μg./24 hr.)	Percent change	Chamber – ground: Special diet Low CO_2 (μg./24 hr.)	Chamber – ground: Special diet High CO_2 (μg./24 hr.)	Percent change CO_2 – ground	Chamber – 32,500 ft.: Special diet Low CO_2 (μg./24 hr.)	Chamber – 32,500 ft.: Special diet High CO_2 (μg./24 hr.)	Percent change CO_2 – altitude	Chamber effect (% change)	Altitude effect (% change)
Epinephrine											
21	5.75	13.64	+137.2	10.19	10.65	+ 4.5	12.34	17.53	+ 42.1	− 25.3	+12.1
22	2.36	7.05	+198.7	10.83	11.47	+ 5.9	12.38	14.08	+ 13.7	+ 53.6	+14.0
23	1.06	4.65	+338.7	3.40	3.54	+ 4.1	5.01	5.28	+ 5.4	− 26.9	+47.4
24	1.54	5.34	+246.8	4.85	6.16	+27.0	3.20	8.01	+150.3	− 9.2	−34.0
25	1.18	1.70	+ 44.1	(9.66)	5.04	(−47.8)	1.32	2.70	+104.5	+468.2	(−85.4)
26	2.60	5.55	+113.5	9.36	10.95	+17.0	12.56	12.70	+ 1.1	+ 68.7	+34.2
27	2.68	4.44	+ 65.7	(16.73)	12.68	(−24.2)	8.24	6.02	− 26.1	+276.8	(−50.7)
28	11.79	17.68	+ 50.0	36.46	37.81	+ 3.7	14.47	22.66	+ 56.6	+106.2	−60.3
Av.			+149.3			+10.4			+ 43.5	+114.0	+15.3
Norepinephrine											
21	56.17	30.50	−45.7	22.05	23.74	+ 7.7	33.50	37.60	+ 12.2	− 27.7	+51.9
22	59.99	38.78	−33.4	44.66	46.29	+ 3.6	36.76	44.22	+ 20.3	+ 15.2	−17.7
23	54.17	45.65	−15.7	39.94	40.76	+ 2.1	29.47	39.88	+ 35.3	− 34.3	−25.8
24	61.67	47.88	−22.4	31.03	39.74	+28.1	37.37	47.1	+ 26.0	− 35.2	+20.5
25	65.46	44.42	−32.1	58.95	60.48	+ 2.6	60.88	63.01	+ 3.5	+ 32.7	+ 3.3
26	75.19	62.92	−16.3	69.55	73.69	+ 6.0	73.48	79.50	+ 8.2	+ 10.5	+ 5.7
27	53.48	42.91	−19.8	42.06	48.05	+14.2	40.44	51.60	+ 27.6	− 2.0	− 3.9
28	68.11	47.32	−30.5	60.79	49.61	−18.4	56.02	59.38	+ 6.0	+ 28.5	− 7.8
Av.			−27.0			+ 5.7			+ 17.4	− 1.5	+ 3.3

TABLE II (Contd.)

Subject	Normal controls: Normal diet (mg./24 hr.)	Normal controls: Special diet (mg./24 hr.)	Percent change	Chamber – ground: Special diet Low CO_2 (mg./24 hr.)	Chamber – ground: Special diet High CO_2 (mg./24 hr.)	Percent change CO_2 – ground	Chamber – 32,500 ft.: Special diet Low CO_2 (mg./24 hr.)	Chamber – 32,500 ft.: Special diet High CO_2 (mg./24 hr.)	Percent change CO_2 – altitude	Chamber effect (% change)	Altitude effect (% change)
						17-Hydroxycorticoids					
21	12.31	10.57	−14.1	10.45	9.48	− 9.3	7.90	6.51	− 17.6	− 1.1	−24.4
22	9.86	7.59	− 8.9	7.51	7.00	− 5.0	7.75	6.08	− 21.5	− 1.1	+ 3.2
23	7.85	8.19	+ 4.3	9.01	9.33	+ 3.5	6.94	4.27	− 38.5	+ 10.0	−23.0
24	9.51	8.97	− 4.2	10.35	8.93	−13.7	11.02	6.76	− 38.7	+ 15.4	+ 6.5
25	12.26	12.32	+ 0.5	14.09	15.62	+10.9	13.29	14.00	+ 5.3	+ 14.4	− 5.7
26	11.98	10.72	−10.5	12.49	13.16	+ 5.4	10.41	9.63	− 7.5	+ 16.5	−16.7
27	8.84	7.47	−15.5	9.19	9.59	+ 4.4	8.66	8.45	− 2.4	+ 23.0	− 5.8
28	10.57	8.71	−17.5	13.00	10.82	−16.8	9.84	9.88	+ 0.4	+ 49.3	−24.3
Av.			− 8.2			− 2.6			− 15.1	+ 15.8	−11.3
						Corticosterone-like hormones					
21	55.75	58.15	+ 4.3	50.32	58.24	+15.7	53.10	53.89	+ 1.5	− 13.5	+ 5.5
22	42.65	40.74	− 4.2	35.01	45.70	+30.5	29.47	42.35	+ 43.7	− 14.1	−15.8
23	31.07	31.38	+ 1.0	25.17	28.99	+15.2	23.15	24.47	+ 5.7	− 19.7	− 8.0
24	36.10	31.66	−12.3	32.48	38.63	+19.0	30.22	31.35	+ 3.7	+ 2.6	− 7.0
25	37.04	26.31	−29.0	53.63	41.98	−21.7	26.69	27.68	+ 3.7	+103.8	−50.4
26	33.53	27.00	−19.5	32.45	28.18	−13.2	23.45	24.09	+ 2.7	+ 20.2	−27.7
27	35.67	25.07	−29.7	41.70	45.52	+ 9.2	25.52	26.51	+ 3.9	+ 66.3	−38.8
28	68.90	48.63	−29.4	97.26	120.6	+24.0	35.17	40.23	+ 14.4	+100.0	−63.8
Av.			−14.9			+ 9.8			+ 9.9	+ 30.7	−25.8

TABLE III

Percent change in hormone excretion

Hormone	Dietary change	CO_2 effects		Chamber effect	Altitude effect
		Ground	Altitude		
Epinephrine	+149.3 (<.01)*	10.4	48.5	114.0 (<.05)	15.3
Norepinephrine	−27.0 (<.01)	5.7	17.4	− 1.5	3.3
17-OHCS	− 8.2	−2.6	−15.1	15.8 (<.05)	−11.3
Corticosterone-like hormones	−14.9 (<.01)	9.8	9.9	30.7 (<.05)	−25.8 (<.01)

*Numbers in parenthesis indicate level of significance.

Norepinephrine. The values obtained for norepinephrine are more puzzling. The hormone values from the two normal-diet control periods were at the same level. Likewise, the excretion of norepinephrine during the three liquid-diet control periods was also essentially the same. However, the special-diet values were less than the values from the normal-diet periods (table II). This effect could not be due to decreased activity since the subjects had the same schedule with the exception of food when they were outside the chamber. Furthermore, there was an increase in norepinephrine excretion after the subject went into the chamber, compared to the initial, liquid-diet period; but there was a decrease when compared to the average value from the three liquid-diet periods (table II). A further indication that the decrease in the norepinephrine excretion was due to the special liquid diet rather than to decreased muscle activity is indicated by the results from a preliminary experiment (unpublished) where two subjects ate precooked, dehydrated food and showed an increase (20.9%) rather than a decrease when the diet started, and a decrease (−12.3%) in excretion due to inactivity when they were inside the chamber. The only time the muscle activity was actually curtailed was when the subjects were inside the chamber. The two subjects on dehydrated food had much less space available for movement since they were in the two-man space cabin simulator and the other 8 subjects were in the converted 20-man indoctrination chamber. During the two periods of high CO_2 concentrations, there were increases in the norepinephrine excretions as compared to the excretions during the two periods with low CO_2 concentrations; so there was undoubtedly a CO_2 effect in the latter study also.

17-Hydroxycorticoids. There was a slight increase in 17-OHCS values when the subjects entered the chamber—undoubtedly caused by apprehension since entering the chamber for the second time did not result in an increase. As a matter of fact, there was decreased 17-OHCS output during the initial part of the 200 mm. Hg portion of the experiment compared to the control values. This decrease may have been caused by a delay in 17-OHCS excretion since it was also observed during the previous prolonged experiment at decreased pressure (19) for a similar period of time.

Corticosterone-like hormones. The corticosterone-like hormones showed essentially the same picture as described for norepinephrine (fig. 2). There were, however, a few differences. The corticosterone values showed an overall increase each time the subjects entered the chamber as compared to the preceding control period, with an added output during the periods of elevated CO_2 concentration. The changes in excretion during the 200 mm. Hg portion of the experiment were of a smaller magnitude.

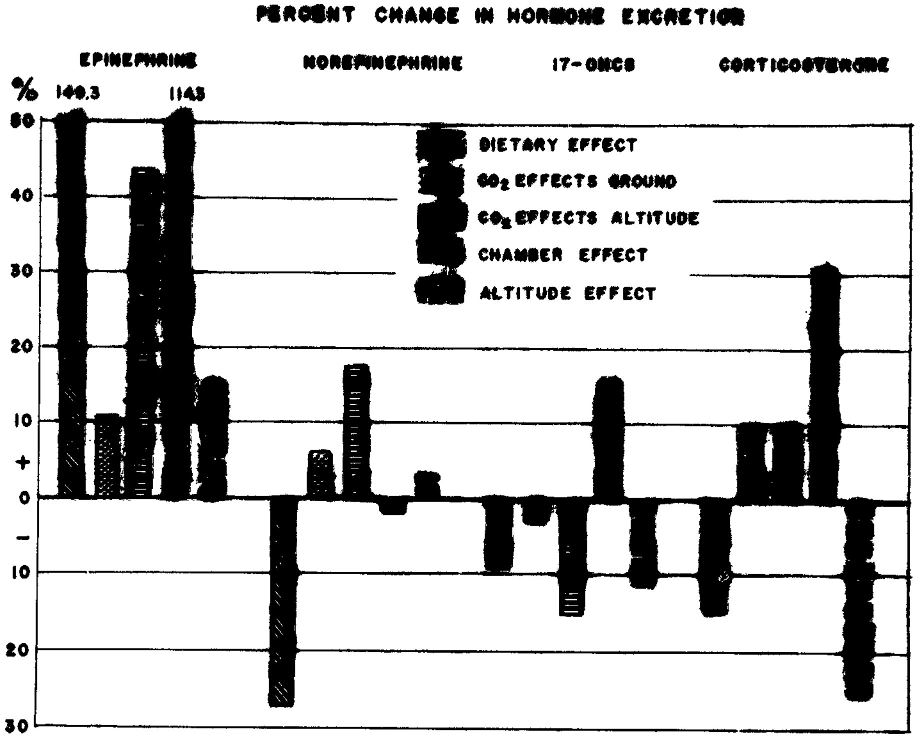


FIGURE 1

Effects of the various experimental parameters on hormone excretion expressed as percent change.

The value obtained during the postexperiment normal-food control period, even though it had increased over the value obtained during the postexperiment liquid-diet period, had not yet reached the equivalent preexperiment control value by the time the experiment (urine collection) was terminated.

CO_2 effects. There is no doubt that the excretions of epinephrine, norepinephrine, and corticosterone-like hormones increased during the periods of high CO_2. Individuals varied in their response to CO_2 (table II), and occasionally a subject showed what appeared to be a negative response. This may have been due to an unknown stress of some kind during the low CO_2 portion of the experiment, or it may have been a real CO_2 effect. King and Schaefer (7) were able to divide subjects into three groups: those with a strong response, those with a modest response, and those with no response. The increase in excretion of hormones during the periods of high CO_2 concentrations could not be reported for the 17-OHCS. As is indicated in table III and figure 2, the excretion of this hormone group dropped as soon as CO_2 was added to the chamber atmosphere. The drop was more marked when CO_2 was added to the 200 mm. Hg atmosphere.

The postexperiment diet values for the 17-OHCS were lower than the values for the two other diet periods. Apparently, there was a slow recovery after the CO_2 exposure and only during the postexperiment, normal-diet period did the excretion exceed the preexperiment normal diet values. There was an increase in the excretion of epinephrine,

norepinephrine, and corticosterone-like hormones during the two periods of high carbon dioxide concentration. From table III, however, it is apparent that while the increases were not statistically significant, they demonstrated a CO_2 effect which was stronger at altitude than at ground level. It cannot be denied that this may also have been due to an anxiety reaction rather than to a physiologic effect of CO_2 since the men claimed that they knew when the CO_2 was admitted to the chamber by the fact that their respiratory functions changed. However, an argument in favor of a real CO_2 effect can be made since the same hormones increased when the CO_2 was administered during the altitude portion of the experiment and returned to the dietary control level as soon as the CO_2 was removed in both cases. It is of interest to note (table III) that the increase in norepinephrine excretion during the periods of high carbon dioxide was less, percentage-wise, than the epinephrine excretion during these periods. This confirms the results obtained by Richardson and Woods (11) and Millar (9), who have shown that it is primarily epinephrine that is released, the concentration of norepinephrine remaining relatively low when the CO_2 concentrations are elevated.

Several investigators (7, 12, 16) have reported on increased adrenal activity in both normal and hypophysectomized rats and guinea pigs. The animals were exposed to 1.5% carbon dioxide at sea level air pressure for up to 91 days. They reported that, after a latent period of 7 days, the adrenal cortical activity was increased as indicated by a decrease in adrenal cholesterol and ascorbic acid content and by marked eosinopenia and lymphopenia. Fortier (6) found that exposure of rats to 15% CO_2 at ground level atmosphere for 3 days produced hyperplasia of the adrenal cortex, indicating a stress response. King and Schaefer (7) exposed 21 males to 1.5% CO_2 for 41 days in a submarine and found an increased adrenal activity based on a decrease in the absolute number of circulating eosinophils and a significant increase in the excretion of urinary 17-ketosteroids. Their values indicate that there may have been a slight delay in the response seen by the excretion of the steroids. This delay in adrenal cortical response seen at the lower concentrations of CO_2 may explain the lack in response seen for 17-OHCS and corticosterone-like hormones to CO_2 in this study, or may indicate that the threshold for a direct CO_2 stimulus on the pituitary-adrenal cortical axis had not been reached. On the other hand, Sechzeer et al. (12) observed an immediate increase in the plasma concentration of epinephrine, norepinephrine, and 17-OHCS when volunteers (males) inspired CO_2 ranging from 7 to 14% in oxygen for 10 to 20 minutes. After 100% O_2 was substituted for the $CO_2—O_2$ mixture, the altered measurements returned to normal over a period of roughly 10 minutes.

At this point, it is pertinent to mention that Tenney (18) observed that higher than normal concentrations of CO_2 initiate the release of epinephrine from the adrenal medulla. This release of epinephrine is responsible for many of the manifestations of respiratory acidosis, and further serves to bring about secondary endocrine and metabolic effects which modify the effector response to both the direct action of CO_2 and epinephrine.

Results from this laboratory (unpublished) show that the subjects had insignificant changes in arterial P_{CO_2} and pH values during the periods of high ambient CO_2 concentrations. Likewise, the potassium values are inconclusive. These points are brought out since several investigators (3, 18) have advanced theories that the initial action of CO_2 is due to changes in blood and cellular pH which then stimulated the sympathetico-adrenal system. Furthermore, because CO_2 directly affects the hepatic cells, potassium is released and it again stimulates the release of epinephrine (5, 16). This topic has been well covered by Tenney (17), who presents evidence of a direct CO_2 effect on the sympathetico-adrenal system. Results of the current study tend to support this theory.

Dietary effect. When the subjects arrived at the USAF School of Aerospace Medicine, they were eating what is considered a normal balanced diet. They were told to continue their usual diet, eliminating only foods containing

TABLE IV

Hormone excretion in 4-day averages

Hormone	Pre-experiment				Chamber – ground				Outside		Chamber – altitude				Postexperiment			
	Normal diet	S.D.	Special diet	S.D.	Low CO_2	S.D.	High CO_2	S.D.	Special diet	S.D.	Low CO_2	S.D.	High CO_2	S.D.	Special diet	S.D.	Normal diet	S.D.
Epinephrine (μg./24 hr.)	4.05	4.66	5.85	4.58	12.17	5.30	12.29	10.80	6.84	5.83	8.69	4.97	10.98	6.90	6.66	6.60	3.44	3.08
Norepinephrine (μg./24 hr.)	59.65	11.69	44.06	9.84	46.05	16.00	47.79	14.75	46.60	10.55	45.99	15.51	52.79	13.93	45.74	12.96	63.06	10.7
17-OHCS (mg./24 hr.)	10.10	2.15	9.14	2.07	10.76	2.25	10.38	2.78	10.28	1.85	9.48	2.08	8.13	3.05	8.11	1.86	10.38	2.43
Corticosterone-like hormones (mg./24 hr.)	43.87	17.90	33.43	7.87	46.00	22.80	50.71	29.80	39.77	15.15	39.85	9.71	33.82	10.62	34.07	14.94	39.19	13.05

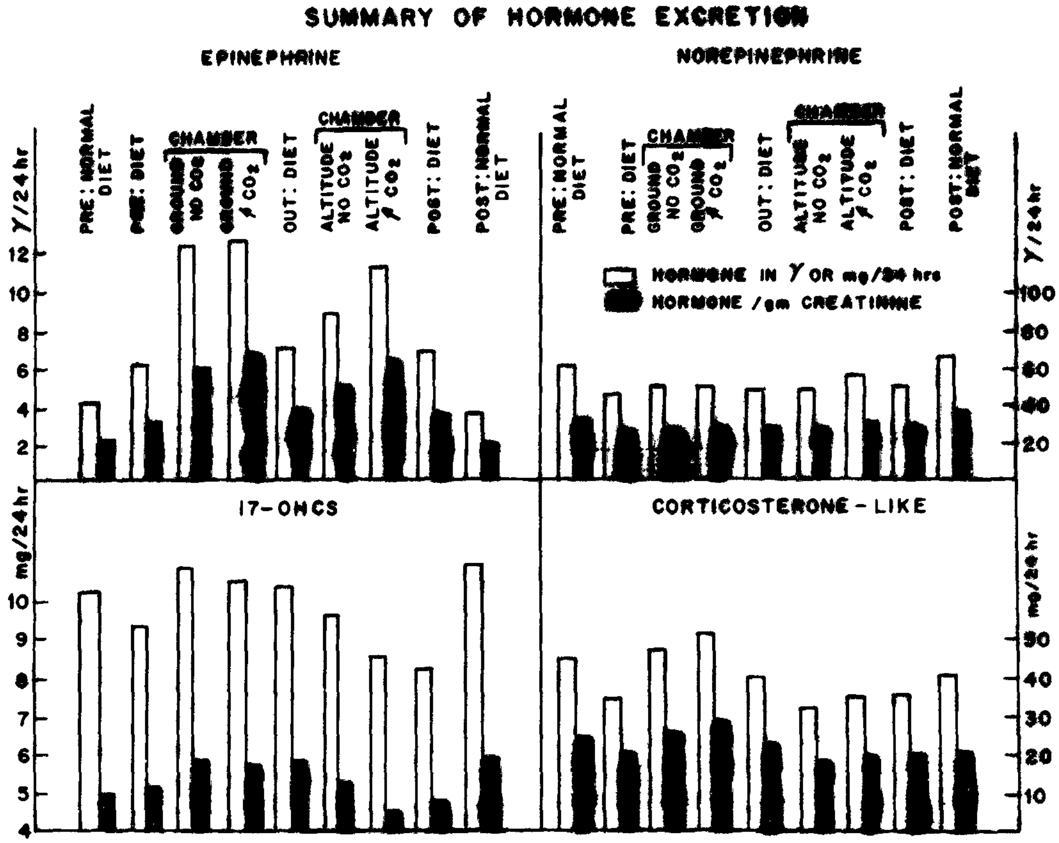


FIGURE 2

Average excretion of catecholamines and steroids from the eight subjects during each of the various experimental parameters.

vanilla and bananas; they were told, also, to abstain from alcoholic beverages. During the next four to five days, baseline data were obtained for 17-OHCS, corticosterone-like hormones, epinephrine, and norepinephrine. Following this initial period, the subjects were given the special liquid diet, and excretions of the above-mentioned hormones were measured. Similar data were obtained after the chamber portion of the experiments. All these control data on normal food were pooled as were data obtained during the three periods on the liquid diet. Results are given in tables II and III and in figure 1. Even though the environmental conditions were as identical as possible, there was a significant increase in the epinephrine excretion ($P < .01$) during the liquid-diet periods over the periods when normal food was consumed. In contrast, the excretions of the other three groups of hormones decreased, norepinephrine and corticosterone-like hormones to a significant degree ($P < .01$). The only exception to this trend was the norepinephrine excretion for the two subjects who had eaten the precooked, dehydrated food in a preliminary study. The reason for this change in hormone excretion is not clearly understood. One possibility is that the special liquid diet caused a change in the ratio of the metabolic constituents and composition in the body, upsetting the normal "traffic" over the enzymatic pathways of fat, protein, and carbohydrate

metabolism and upsetting also the pathways of salt and water metabolism. Also, it is of interest to note that these two subjects in the preliminary study only had a 17.8% increase in the epinephrine excretion while the other eight subjects averaged a 149.3% increase in the epinephrine excretion. A psychologic effect may be excluded since the levels for the pre-, mid-, and postexperimental liquid-diet periods are almost identical (fig. 2; table IV). This fact also indicates that the body retained this new "basal" level of excretion since the hormone values did not return to original normal-diet levels until the liquid diet was discontinued; this further indicates that the changes in hormone excretions were really due to the change in metabolic makeup.

The special liquid diet may have caused the drop in 17-OHCS excretion, since once the subjects started on the diet, the excretions dropped. The increased urinary output of these hormones, occurring when the subjects entered the chamber, is explainable as apprehension and familiarization strain. After the initial chamber increase, there was a continuous decline regardless of experimental conditions until the special liquid diet was discontinued. The reason for these changes—apparently due to the special liquid diet—warrants further study.

4. SUMMARY

When healthy male subjects were exposed to 3% CO_2 at 700 mm. Hg in an altitude chamber for 4 days and to an equivalent tracheal P_{CO_2} at 200 mm. Hg, there was an effect on the excretion of epinephrine, norepinephrine, 17-OHCS, and corticosterone-like hormones. In the case of epinephrine, norepinephrine, and corticosterone-like hormones, there was an increased urinary output while for 17-OHCS there was a decreased output. The concentration of CO_2 may not have been high enough, or the duration of exposure may not have been long enough to show a significant change in all cases, but at least a trend is evident.

The special liquid diet supplied to the subjects appeared to change the level of excretion of the above-mentioned hormones. The excretion of epinephrine was increased on this diet, while the excretion of the other three hormone groups was decreased. This change may be due to an altered ratio of metabolites in the enzymatic pathways and therefore the requirement for these hormones. However, the organism adjusted to the new diet, as evidenced by the new level of excretion during the three liquid dietary control periods. The dietary regimen seemed to have a more significant effect on the hormone excretions than did CO_2 under these experimental conditions.

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SAM-TDR-63-63. EFFECTS OF HIGH CONCENTRATIONS OF CARBON DIOXIDE AND DIET ON URINARY EXCRETION OF STEROIDS AND CATECHOLAMINES. Aug. 63, 12 pp. incl. illus., tables, 21 refs.

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